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General Physiology is the study of biological mechanisms through analytical investigations, which decipher the molecular and cellular mechanisms underlying biological function at all levels of organization.

The mission of the *Journal of General Physiology* is to publish articles that elucidate important biological, chemical, or physical mechanisms of broad physiological significance.

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Cover picture: Four bifurcation diagrams and corresponding time simulations of bursting made with a Chay–Keizer model of a cell. In the top of each pair of panels, the solid black line represents stable states of V_m as a function of (clamped) Ca, the dashed and dotted lines represent unstable equilibria and unstable oscillations, and the blue lines represent burst trajectories. The bottom of each pair of panels shows the corresponding time-dependent changes in V_m with Ca free to vary. Upper left: square wave without spikes; upper right: β cell–like bursting; lower left: pituitary-like bursting; lower right: bursting without bistability but with two slow variables, as in the R15 neuron of Aplysia (see commentary by Sherman, 13–19).

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Cover picture: Antibiotic resistance is a game of tic-tac-toe: Harvested *Xenopus laevis* oocytes (O's) visibly damaged (black foci on animal pole) by multi-drug–resistant bacteria; scanning electron micrographs (X's) of the multi-drug–resistant bacteria on the oocyte's surface that are susceptible to a ciprofloxacin/amikacin antibiotic cocktail. Judicious antibiotic usage should prevent further drug resistance while providing healthy oocytes for the investigation of ion transport proteins (see communication by O'Connell et al., 271–277).

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Cover picture: Modification of the cytoplasmic, carboxyl-terminal domain (CT) of connexin26 affects modulation of channel activity by *taurine* (left, from top: orbital structure, electrostatic potential, local ionization potential). Energy-minimized conformations of the native CT (center) with a four amino acid addition (right) are shown. NMR shows that taurine interacts only with the cytoplasmic loop domain (CL), not the CT. In the presence of taurine, the pore closes; the four amino acid extension causes pore narrowing. Results suggest that CL–CT interaction affects gating, and that taurine modifies this interaction (see article by Locke et al., 321–339).

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Cover picture: Scheme depicting a submembrane ATP-ADP pool, restricted diffusionally from bulk cytoplasmic enzymes and nucleotides in intact human red blood cells. Discrepancies between measured and predicted nucleotide changes induced by Ca^{2+} pump–saturating calcium loads can be explained by the hypothesis that the submembrane ATP pool is the immediate source of energy for the plasma membrane sodium and calcium pumps (see article by Tiffert and Lew, 381–391).

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Cover picture: (Left) The grand canonical Monte Carlo Brownian dynamics (GCMC/BD) system used to simulate ion permeation through molecular dynamics–equilibrated and non-equilibrated structural models of connexin-26 (Cx26) hemichannels. (Right) Depiction of sites at which charges were changed in the GCMC/BD studies to mimic the effects of previously reported MS-identified Cx26 protein modifications. Blue, N-acetylation of Met1; red, acetylation of lysine residue (K15) in the NT; green, acetylation of six internal lysine residues in CL; orange, γ-carboxylation of three glutamates (see article by Kwon et al., 475–493).

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Cover picture: The energy landscapes in the left and center panels reveal the importance of residue Phe103 as an allosteric link between the activation and inactivation gates of the KcsA potassium channel. As the intracellular gate transitions from closed (left) to open (center), the minimum of the energy landscape shifts to favor the rotameric state of Phe103 observed in the open crystal conformation. The right panel illustrates the steric clash that causes the Phe103 to change conformation after the intracellular gate opens (see article by Pan et al., 571–580).